





#### **CLAIMS**

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A compound of the formula

AXX

5 /B

wherein

A is  $(CH_2)_m$ , m being from 1 to 3;

B is (CH<sub>2</sub>)<sub>n</sub>, n being from 1 to 3;

x is from 0 to 2;

R<sup>1</sup> is C<sub>1</sub> to C<sub>10</sub> hydrocarbyl, in which up to 2 carbon atoms may be replaced by O, S or N, and up to 2 hydrogen atoms may be replaced by halogen;

R<sup>2</sup> is H or C<sub>1</sub> to C<sub>15</sub> hydrocarbyl, in which up to 3 carbon atoms may be replaced by O, S or N, and up to 3 hydrogen atoms may be replaced by halogen;

 $R^3$  is absent when -Y-Z- $R^2$  is attached to W, or is H or  $C_1$  to  $C_7$  hydrocarbyl when -Y-Z- $R^2$  is not attached to W;

W is nitrogen;

X is -CH<sub>2</sub>-, -O- or -NR<sup>4</sup>-, R<sup>4</sup> being H or C<sub>1</sub> to C<sub>3</sub> alkyl;

Y replaces a hydrogen atom on any of A, B, W and X, and is C<sub>2</sub> to C<sub>10</sub> alkylene, in which one non-terminal carbon atom may be replaced by O; and

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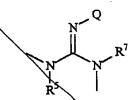
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Z is

wherein R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are independently H or C<sub>1</sub> to C<sub>15</sub> hydrocarbyl, in which up to 3 carbon atoms may be replaced by O or N, and up to 3 hydrogen AMENDED SHEET

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atoms may be replaced by halogen, and Q is H or methyl, or Q is linked to R<sup>5</sup> or R to form a five-membered ring or Q is linked to R<sup>2</sup> to form a six-membered ring, provided that when Z is



at least one of R<sup>5</sup> and R<sup>7</sup> is aryl(C<sub>1</sub> to C<sub>3</sub>)alkyl or cycloalkyl(C<sub>1</sub> to C<sub>3</sub>)alkyl, optionally substituted by halo;

or a pharmaceutically acceptable salt thereof.

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A compound according to claim 1 wherein R<sup>2</sup> is selected from alkyl, aryl, arylalkyl, cycloalkyl and cycloalkylalkyl, wherein alkyl moieties are optionally substituted by halo, and aryl groups are optionally substituted by C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>4</sub> alkoxy or halo.

3. A compound according to claim 1 wherein R<sup>2</sup> is selected from phenyl, halophenyl, benzyl, halobenzyl, phenylethyl, halophenylethyl, phenylpropyl, halophenylpropyl, halophenylbutyl, tolyl, methoxybenzyl, trifluoromethylbenzyl, halo-methoxybenzyl, phenylbenzyl, adamantanemethyl, adamantanepropyl, cyclohexanemethyl, cyclohexaneethyl, and naphthyl.

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- 4. A compound according to any of claims 1 to 3 wherein x is 0.
- 5. A compound according to any of claims 1 to 3 wherein x is 1 or 2, and R<sup>1</sup> is selected from hydroxy, C<sub>1</sub> to C<sub>9</sub> alkoxy (optionally substituted by halo), C<sub>1</sub> to C<sub>9</sub> cycloalkylalkoxy (wherein the cycloalkyl group is optionally substituted by C<sub>1</sub> to C<sub>4</sub> alkyl or halo, and the alkoxy group is optionally substituted by halo), arylalkoxy (wherein the aryl group is optionally substituted by C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy or halo, and the alkoxy group is optionally substituted by halo) and C<sub>1</sub> to C<sub>9</sub> alkylamino wherein the alkyl group is optionally substituted by halo.



gus A 1>

A compound according to any preceding claim wherein R<sup>3</sup> is H, C<sub>1</sub> to C<sub>7</sub> alkyl or benzyl

- 7. A compound according to any preceding claim wherein R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are independently selected from H, aryl(C<sub>1</sub> to C<sub>3</sub>)alkyl and cycloalkyl(C<sub>1</sub> to C<sub>3</sub>)alkyl, and are optionally substituted by halo.
  - 8. A compound according to any preceding claim wherein Y is propylene, butylene, pentylene, hexylene, heptylene, octylene or nonylene.

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- 9. A compound according to any preceding claim wherein  $m+n \ge 3$ .
- 10. A compound according to claim 8, wherein  $m+n \ge 3$ ,  $Z-R^2$  is

15 and R<sup>5</sup> is benzyl or halobenzyl.

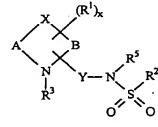
11. A compound according to any preceding claim, for use in therapy.

90% AS>

- 12. A compound which is degraded in vivo to yield a compound according to any of claims Nto 10.
- 13. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any of claims 1 to 10, and a physiologically acceptable diluent or carrier.

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14. A method of making a compound of the formula



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wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula R<sup>2</sup>SO<sub>2</sub>Cl with a compound of the formula

$$A \xrightarrow{X}_{B}^{(R^1)_x} Y - N \xrightarrow{R^5}_{H}$$

- 5 wherein R<sup>3A</sup> is C<sub>1</sub> to C<sub>7</sub> hydrocarbyl or a protecting group.
  - 15. A method of making a compound of the formula

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

with a compound of the formula Cl-Y-NH-SO<sub>2</sub>-R<sup>2</sup>.

16. A method of making a compound of the formula

$$\begin{array}{c|c}
X & (R^1)_{\lambda} \\
B & R^5 & R \\
N & Y - N & N \\
R^3 & O & O
\end{array}$$

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

(wherein R<sup>3A</sup> is C<sub>1</sub> to C<sub>7</sub> hydrocarbyl or a protecting group and Pr is a protecting group) with a compound of the formula R<sup>2</sup>Br, and reacting the product with R<sup>5</sup>Br when R<sup>5</sup> is not hydrogen.

17. A method of making a compound of the formula

$$\begin{array}{c|c}
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wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

$$\begin{array}{c}
X \\
X \\
B \\
Y - OH \\
R^{3A}
\end{array}$$

(wherein R<sup>3A</sup> is C<sub>1</sub> to C<sub>7</sub> hydrocarbyl or a protecting group) with a compound of the formula R<sup>2</sup>-NH-SO<sub>2</sub>-NH-Pr, wherein Pr is a protecting group, and reacting the product with R<sup>6</sup>Br when R<sup>6</sup> is not hydrogen.

15 18. A method of making a compound of the formula

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

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$$A \xrightarrow{X} B \\ Y = NHR^{5}$$

(wherein  $R^{3A}$  is  $C_1$  to  $C_7$  hydrocarbyl or a protecting group) with a compound of the formula  $R^2R^6NH$  and sulfamide.

#### 5 19. A method of making a compound of the formula

$$A \xrightarrow{X}_{B}_{Q^{2}} S \xrightarrow{Q^{2}}_{R^{6}} R^{2}$$

wherein A, B, x,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^6$  and X are as recited in claim 1 and  $Y^2$  is a bond or  $C_1$  to  $C_8$  alkylene, said method comprising the step of reacting a compound of the formula

$$\begin{array}{c|c}
X & (R^{1})_{x} \\
X & & \\
X & & \\
N & & Y-CHO
\end{array}$$

10 (wherein R<sup>3A</sup> is C<sub>1</sub> to C<sub>7</sub> hydrocarbyl or a protecting group) with a compound of the formula

wherein Pr is a protecting group, reducing the reaction product, and (when R<sup>6</sup> is not hydrogen) reacting the reduced product with R<sup>6</sup>Br.

## 20. A method of making a compound of the formula



wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>7</sup>, Q, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

$$A \xrightarrow{X}_{B}^{(R^1)_x}$$

$$Y - NHR^5$$

$$R^{3A}$$

with a compound of the formula

wherein  $Q^1$ ,  $R^{2A}$ ,  $R^{3A}$ , and  $R^{7A}$  are any of the groups defined for Q,  $R^2$ ,  $R^3$ , and  $R^7$ , respectively, or protecting groups.

#### 21. A method of making a compound of the formula

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wherein A, B, x,  $R^1$ ,  $R^2$ , and X are as recited in claim 1 and  $Y^1$  is a  $C_1$  to  $C_9$  alkylene group, said method comprising the step of reacting a compound of the formula

(wherein Pr<sup>1</sup> and Pr<sup>2</sup> are protecting groups) with a compound of the formula



22. A method of making a compound of the formula

$$\begin{array}{c}
X \\
X \\
B \\
Y - N \\
R^{3}
\end{array}$$

$$\begin{array}{c}
X \\
Y - N \\
R^{2}
\end{array}$$

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

$$A \xrightarrow{X} B \\ N \\ Y - NHR^{5}$$

(wherein  $R^{3A}$  is  $C_1$  to  $C_7$  hydrocarbyl or a protecting group) with a compound of the formula

$$R^2-S_{O-Me}^{"O}$$

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23. A method of making a compound of the formula

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, and X are as recited in claim 1 and Y<sup>1</sup> is a C<sub>1</sub> to C<sub>9</sub> alkylene group, said method comprising the step of reacting a compound of the formula

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$$A \underbrace{\begin{array}{c} X \\ X \\ B \end{array}}_{H}^{(R^1)_{x}}$$

with a compound of the formula R<sup>2</sup>-SO<sub>2</sub>-Y<sup>1</sup>-CHO.

### 24. A method of making a compound of the formula

$$\begin{array}{c|c}
X & (R^1)_x \\
B & & \\
N & & NQ \\
Y & & & \\
Y & & & \\
R^5 & & R^2
\end{array}$$

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup>, R<sup>7</sup>, Q, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

with a compound of the formula

$$\begin{array}{c|c}
R^{5A} & & Q^{1} \\
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wherein V is  $C_1$  to  $C_9$  alkylene, and  $Q^1$ ,  $R^{2A}$ ,  $R^{5A}$  and  $R^{7A}$  are any of the groups defined for Q,  $R^2$ ,  $R^5$  and  $R^7$ , respectively, or a protecting group.

# 25. A method of making a compound of the formula



$$A \xrightarrow{X} B \\ N \\ R^{5}$$

$$N \\ N \\ N \\ N \\ R^{7}$$

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup>, R<sup>7</sup>, Q, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

$$A \xrightarrow{X \\ B} B$$

5 with a compound of the formula

wherein L is a leaving group, and  $Q^1$ ,  $R^{2A}$ ,  $R^{5A}$  and  $R^{7A}$  are any of the groups defined for Q,  $R^2$ ,  $R^5$  and  $R^7$ , respectively, or a protecting group.

10 26. A method of making a compound of the formula

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup>, X and Y are as recited in claim 1, said method comprising the step of reacting a compound of the formula

$$A \xrightarrow{X}_{B}^{(\mathbb{R}^{1})_{x}}$$

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with a compound of the formula

wherein V is  $C_1$  to  $C_9$  alkylene, and  $R^{2A}$  and  $R^{5A}$  are any of the groups recited for  $R^2$  and  $R^5$ , respectively, or a protecting group.

27. A method of making a compound of the formula

wherein A, B, x, R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup>, X and Y are as recited in claim 1 (provided that the moiety

constitutes a group falling within the definition of R<sup>6</sup>), said method comprising the step of reacting a compound of the formula

$$A \xrightarrow{X \\ B} B$$

with a compound of the formula

$$\begin{array}{c|cccc}
R^{5A} & O & O \\
R^{5A} & N & S & N \\
O & V & V & O
\end{array}$$

wherein V is C<sub>1</sub> to C<sub>9</sub> alkylene, and R<sup>2A</sup> and R<sup>5A</sup> are any of the groups recited for R<sup>2</sup> and R<sup>5</sup>, respectively, or a protecting group.

sub A3>

28. The use of an H<sub>3</sub> receptor ligand in the manufacture of a medicament for modifying H<sub>3</sub> receptor activity in a patient, said H<sub>3</sub> receptor ligand being a compound of the formula

$$A \xrightarrow{X} (R^1)_x$$

$$Y - Z - R^2$$

$$R^3$$

5 wherein

A is (CH<sub>2</sub>)<sub>m</sub>, m being from 1 to 3;

B is (CH<sub>2</sub>)<sub>n</sub>\n being from 1 to 3;

x is from 0 to 2;

 $R^1$  is  $C_1$  to  $C_{10}$  hydrocarbyl, in which up to 2 carbon atoms may be replaced by O, S or N and up to 2 hydrogen atoms may be replaced by halogen;

R<sup>2</sup> is H or C<sub>1</sub> to C<sub>1</sub> hydrocarbyl, in which up to 3 carbon atoms may be replaced by O, S or N, and up to 3 hydrogen atoms may be replaced by halogen;

 $R^3$  is absent when  $-Y-Z R^2$  is attached to W, or is H or  $C_1$  to  $C_7$  hydrocarbyl when  $-Y-Z-R^2$  is not attached to W;

W is nitrogen;

X is -CH<sub>2</sub>-, -O- or -NR<sup>4</sup>-, R being H or C<sub>1</sub> to C<sub>3</sub> alkyl;

Y replaces a hydrogen atom on any of A, B, W and X, and is C<sub>2</sub> to C<sub>10</sub> alkylene, in which one non-terminal carbon atom may be replaced by O; and

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Z is

$$-N-S$$

500 A3>

wherein R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are independently H or C<sub>1</sub> to C<sub>15</sub> hydrocarbyl, in which up to 3 carbon atoms may be replaced by O or N, and up to 3 hydrogen atoms may be replaced by halogen, and Q is H or methyl, or Q is linked to R<sup>5</sup> or R<sup>7</sup> to form a five-membered ring or Q is linked to R<sup>2</sup> to form a six-membered ring,

or a pharmaceutically acceptable salt thereof.

add B2

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